

65823 SEQUENCE LISTING

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<110> Sato, Taka-Aki
<120> METHOD OF PREPARING A PROTEIN ARRAY BASED ON
      BIOCHEMICAL PROTEIN-PROTEIN INTERACTION
<130> 65823/JPW/PT
<140> Not Yet Known
<141> 2002-03-04
<160> 34
<170> PatentIn Ver. 2.1
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<222> (1)
<223> Xaa=Gly, Ser, Ala or Glu
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<223> Xaa=Phe, Ile or Leu
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Xaa Leu Gly Xaa
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<222> (1)
<223> Xaa=Lys, Arg or Gln
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<222> (2)..(5)
<223> Xaa=any amino acid, up to 2 Xaa may be missing
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<223> Xaa=Val, Ile or Leu
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<210> 5

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Asp Ser Glu Asn Ser Asn Phe Arg Asn Glu Ile Gln Ser Leu Val
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Ser Ile Ser Asn Ser Arg Asn Glu Asn Glu Gly Gln Ser Leu Glu
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Ser Thr Pro Asp Thr Gly Asn Glu Asn Glu Gly Gln Cys Leu Glu
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Glu Ser Leu Val
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 Arg Asn Glu Ile Gln Ser Leu Val
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20 25 30

Pro Thr Gly Leu Tyr Thr His Ser Gly Glu Cys Cys Lys Ala Cys Asn 35 40 45

Leu Gly Glu Gly Val Ala Gln Pro Cys Gly Ala Asn Gln Thr Val Cys 50 55 60

Glu Pro Cys Leu Asp Ser Val Thr Phe Ser Asp Val Val Ser Ala Thr 65 70 75 80

Glu Pro Cys Lys Pro Cys Thr Glu Cys Val Gly Leu Gln Ser Met Ser 85 90 95

Ala Pro Cys Val Glu Ala Asp Asp Ala Val Cys Arg Cys Ala Tyr Gly
100 105 110

Tyr Tyr Gln Asp Glu Thr Thr Gly Arg Cys Glu Ala Cys Arg Val Cys 115 120 125

Glu Ala Gly Ser Gly Leu Val Phe Ser Cys Gln Asp Lys Gln Asn Thr 130 135 140

Val Cys Glu Glu Cys Pro Asp Gly Thr Tyr Ser Asp Glu Ala Asn His 145 150 155 160

Val Asp Pro Cys Leu Pro Cys Thr Val Cys Glu Asp Thr Glu Arg Gln
165 170 175

Leu Arg Glu Cys Thr Arg Trp Ala Asp Ala Glu Cys Glu Glu Ile Pro 180 185 190

65823 Gly Arg Trp Ile Thr Arg Ser Thr Pro Pro Glu Gly Ser Asp Ser Thr 200 Ala Pro Ser Thr Gln Glu Pro Glu Ala Pro Pro Glu Gln Asp Leu Ile 215 Ala Ser Thr Val Ala Gly Val Val Thr Thr Val Met Gly Ser Ser Gln 230 Pro Val Val Thr Arg Gly Thr Thr Asp Asn Leu Ile Pro Val Tyr Cys 250 Ser Ile Leu Ala Ala Val Val Gly Leu Val Ala Tyr Ile Ala Phe Lys Arg Trp Asn Ser Cys Lys Gln Asn Lys Gly Gly Ala Asn Ser Arg 280 Pro Val Asn Gln Thr Pro Pro Pro Glu Gly Glu Lys Ile His Ser Asp 295 Ser Gly Ile Ser Val Asp Ser Gln Ser Leu His Asp Gln Gln Pro His Thr Gln Thr Ala Ser Gly Gln Ala Leu Lys Gly Asp Gly Leu Tyr 330 Ser Ser Leu Pro Pro Ala Lys Arg Glu Glu Val Glu Lys Leu Leu Asn Gly Ser Ala Gly Asp Thr Trp Arg His Leu Ala Gly Glu Leu Gly Tyr 360 Gln Pro Glu His Ile Asp Ser Phe Thr His Glu Ala Cys Pro Val Arg 375 Ala Leu Leu Ala Ser Trp Ala Thr Gln Asp Ser Ala Thr Leu Asp Ala Leu Leu Ala Ala Leu Arg Arg Ile Gln Arg Ala Asp Leu Val Glu Ser Leu Cys Ser Glu Ser Thr Ala Thr Ser Pro Val 420

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<212> PRT

<213> human

Met Asn Arg Gly Val Pro Phe Arg His Leu Leu Val Leu Gln Leu

Ala Leu Leu Pro Ala Ala Thr Gln Gly Lys Lys Val Val Leu Gly Lys

Lys Gly Asp Thr Val Glu Leu Thr Cys Thr Ala Ser Gln Lys Lys Ser Page 8

| lle | Gln 50 | Phe | His | Trp | Lys | Asn 55 | Ser | Asn | Gln | Ile | Lys | Ile | Leu | Gly | Asn |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Gln 65 | Gly | Ser | Phe | Leu | Thr 70 | Lys | Gly | Pro | Ser | Lys 75 | Leu | Asn | Asp | Arg | Ala 80 |
| Asp | Ser | Arg | Arg | Ser 85 | Leu | Trp | Asp | Gln | Gly 90 | Asn | Phe | Pro | Leu | Ile 95 | Ile |
| Lys | Asn | Leu | Lys 100 | Ile | Glu | Asp | Ser | Asp 105 | Thr | Tyr | Ile | Cys | Glu 110 | Val | Glu |
| Asp | Gln | Lys 115 | Glu | Glu | Val | Gln | Leu 120 | Leu | Val | Phe | Gly | Leu 125 | Thr | Ala | Asn |
| Ser | Asp 130 | Thr | His | Leu | Leu | Gln 135 | Gly | Gln | Ser | Leu | Thr 140 | Ile | Thr | Leu | Glu |
| Ser 145 | Pro | Pro | Gly | Ser | Ser 150 | Pro | Ser | Val | Gln | Cys 155 | Arg | Ser | Pro | Arg | Gly 160 |
| Lys | Asn | Ile | Gln | Gly 165 | Gly | Lys | Thr | Leu | Ser 170 | Val | Ser | Gln | Leu | Glu 175 | Leu |
| Gln | Asp | Ser | Gly 180 | Thr | Trp | Thr | Cys | Thr 185 | Val | Leu | Gln | Asn | Gln 190 | Lys | Lys |
| Val | Glu | Phe 195 | Lys | Ile | Asp | Ile | Val 200 | Val | Leu | Ala | Phe | Gln 205 | Lys | Ala | Ser |
| Ser | Ile 210 | Val | Tyr | Lys | Lys | Glu 215 | Gly | Glu | Gln | Val | Glu 220 | Phe | Ser | Phe | Pro |
| Leu 225 | Ala | Phe | Thr | Val | Glu 230 | Lys | Leu | Thr | Gly | Ser 235 | Gly | Glu | Leu | Trp | Trp 240 |
| Gln | Ala | Glu | Arg | Ala 245 | Ser | Ser | Ser | Lys | Ser 250 | Trp | Ile | Thr | Phe | Asp 255 | Leu |
| Lys | Asn | Lys | Glu 260 | Val | Ser | Val | Lys | Arg 265 | Val | Thr | Gln | Asp | Pro 270 | Lys | Leu |
| Gln | Met | Gly 275 | Lys | Lys | Leu | Pro | Leu 280 | His | Leu | Thr | Leu | Pro 285 | Gln | Ala | Leu |
| Pro | Gln 290 | Tyr | Ala | Gly | Ser | Gly 295 | Asn | Leu | Thr | Leu | Ala 300 | Leu | Glu | Ala | Lys |
| Thr 305 | Gly | Lys | Leu | His | Gln 310 | Glu | Asn | Val | Leu | Val 315 | Val | Met | Arg | Ala | Thr 320 |
| Gln | Leu | Gln | Lys | Asn 325 | Leu | Thr | Cys | Glu | Val 330 | Trp | Gly | Pro | Thr | Ser 335 | Pro |
| .Lys | Leu | Met | Leu 340 | Ser | Leu | Lys | Leu | Glu 345 | Asn | Lys | Glu | Ala | Lys 350 | Val | Ser |

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Lys Arg Glu Lys Ala Val Trp Val Leu Asn Pro Glu Ala Gly Met Trp 355 360 365

Gln Cys Leu Leu Ser Asp Ser Gly Gln Val Leu Leu Glu Ser Asn Ile 370 375 380

Lys Val Leu Pro Thr Trp Ser Thr Pro Val Gln Pro Met Ala Leu Ile 385 390 395 400

Val Leu Gly Gly Val Ala Gly Leu Leu Phe Ile Gly Leu Gly Ile 405 410 415

Phe Phe Cys Val Arg Cys Arg His Arg Arg Arg Gln Ala Glu Arg Met
420 425 430

Ser Gln Ile Lys Arg Leu Leu Ser Glu Lys Lys Glu Cys Gln Cys Pro 435 440 445

His Arg Phe Gln Lys Thr Cys Ser Pro Ile 450 455

<210> 26

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<212> PRT

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Met Asn Ser Gly Val Ala Met Lys Tyr Gly Asn Asp Ser Ser Ala Glu 1 5 10 15

Leu Ser Glu Leu His Ser Ala Ala Leu Ala Ser Leu Lys Gly Asp Ile 20 25 30

Val Glu Leu Asn Lys Arg Leu Gln Gln Thr Glu Arg Glu Asp Leu Leu 35 40 45

Glu Lys Lys Leu Ala Lys Ala Gln Cys Glu Gln Ser His Leu Met Arg 50 60

Glu His Glu Asp Val Gln Glu Arg Thr Thr Leu Arg Tyr Glu Glu Arg 65 70 75 80

Ile Thr Glu Leu His Ser Val Ile Ala Glu Leu Asn Lys Lys Ile Asp 85 90 95

Arg Leu Gln Gly Thr Thr Ile Arg Glu Glu Asp Glu Tyr Ser Glu Leu 100 105 110

Arg Ser Glu Leu Ser Gln Ser Gln His Glu Val Asn Glu Asp Ser Arg 115 120 125

Ser Met Asp Gln Asp Gln Thr Ser Val Ser Ile Pro Glu Asn Gln Ser 130 140

Thr Met Val Thr Ala Asp Met Asp Asn Cys Ser Asp Ile Asn Ser Glu 145 150 155 160

Leu Gln Arg Val Leu Thr Gly Leu Glu Asn Val Val Cys Gly Arg Lys Page 10

| T | Cor | Cor | Cira | cor | T 011 | 202 | Val | 777 | Glu | Val | λen | λνα | Hic | Tle | Glu |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| ьys | ser | ser | 180 | ser | ьeu | ser | vai | Ala 185 | GIU | vai | Asp | Arg | 190 | 116 | GIU |
| Gln | Leu | Thr 195 | Thr | Ala | Ser | Glu | His 200 | Cys | Asp | Leu | Ala | Ile 205 | Lys | Thr | Val |
| Glu | Glu 210 | Ile | Glu | Gly | Val | Leu 215 | Gly | Arg | Asp | Leu | Tyr 220 | Pro | Asn | Leu | Ala |
| Glu 225 | Glu | Arg | Ser | Arg | Trp 230 | Glu | Lys | Glu | Leu | Ala 235 | Gly | Leu | Arg | Glu | Glu 240 |
| Asn | Glu | Ser | Leu | Thr 245 | Ala | Met | Leu | Cys | Ser 250 | Lys | Glu | Glu | Glu | Leu 255 | Asn |
| Arg | Thr | Lys | Ala 260 | Thr | Met | Asn | Ala | Ile 265 | Arg | Glu | Glu | Arg | Asp 270 | Arg | Leu |
| Arg | Arg | Arg 275 | Val | Arg | Glu | Leu | Gln 280 | Thr | Arg | Leu | Gln | Ser 285 | Val | Gln | Ala |
| Thr | Gly 290 | Pro | Ser | Ser | Pro | Gly 295 | Arg | Leu | Thr | Ser | Thr 300 | Asn | Arg | Pro | Ile |
| Asn 305 | Pro | Ser | Thr | Gly | Glu 310 | Leu | Ser | Thr | Ser | Ser 315 | Ser | Ser | Asn | Asp | Ile 320 |
| Pro | Ile | Ala | Lys | Ile 325 | Ala | Glu | Arg | Val | Lys 330 | Leu | Ser | Lys | Thr | Arg 335 | Ser |
| Glu | Ser | Ser | Ser 340 | Ser | Asp | Arg | Pro | Val 345 | Leu | Gly | Ser | Glu | Ile 350 | Ser | Ser |
| Ile | Gly | Val 355 | Ser | Ser | Ser | Val | Ala 360 | Glu | His | Leu | Ala | His 365 | Ser | Leu | Gln |
| Asp | Cys 370 | Ser | Asn | Ile | Gln | Glu 375 | Ile | Phe | Gln | Thr | Leu 380 | Tyr | Ser | His | Gly |
| Ser 385 | Ala | Ile | Ser | Glu | Ser 390 | Lys | Ile | Arg | Glu | Phe 395 | Glu | Val | Glu | Thr | Glu 400 |
| Arg | Leu | Asn | Ser | Arg 405 | Ile | Glu | His | Leu | Lys 410 | Ser | Gln | Asn | Asp | Leu 415 | Leu |
| Thr | Ile | Thr | Leu 420 | Glu | Glu | Cys | Lys | Ser 425 | Asn | Ala | Glu | Arg | Met 430 | Ser | Met |
| Leu | Val | Gly 435 | Lys | Tyr | Glu | Ser | Asn 440 | Ala | Thr | Ala | Leu | Arg 445 | Leu | Ala | Leu |
| Gln | Tyr 450 | Ser | Glu | Gln | Cys | Ile 455 | Glu | Ala | Tyr | Glu | Leu 460 | Leu | Leu | Ala | Leu |
| Ala 465 | Glu | Ser | Glu | Gln | Ser 470 | Leu | Ile | Leu | Gly | Gln 475 | Phe | Arg | Ala | Ala | Gly 480 |
| | | | | | | | | | | | | | | | |

| Val | Gly | Ser | Ser | Pro 485 | Gly | Asp | Gln | Ser | | 658∠ Asp | | Asn | Ile | Thr 495 | Gln |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|
| Met | Leu | Lys | Arg 500 | Ala | His | Asp | Cys | Arg 505 | Lys | Thr | Ala | Glu | Asn 510 | Ala | Ala |
| Lys | Ala | Leu 515 | Leu | Met | Lys | Leu | Asp 520 | Gly | Ser | Cys | Gly | Gly 525 | Ala | Phe | Ala |
| Val | Ala 530 | Gly | Cys | Ser | Val | Gln 535 | Pro | Trp | Glu | Ser | Leu 540 | Ser | Ser | Asn | Ser |
| His 545 | Thr | Ser | Thr | Thr | Ser 550 | Ser | Thr | Ala | Ser | Ser 555 | Cys | Asp | Thr | Glu | Phe 560 |
| Thr | Lys | Glu , | Asp | Glu 565 | Gln | Arg | Leu | Lys | Asp 570 | Tyr | Ile | Gln | Gln | Leu 575 | Lys |
| Asn | Asp | Arg | Ala 580 | Ala | Val | Lys | Leu | Thr 585 | Met | Leu | Glu | Leu | Glu 590 | Ser | Ile |
| His | Ile | Asp 595 | Pro | Leu | Ser | Tyr | Asp 600 | Val | Lys | Pro | Arg | Gly 605 | Asp | Ser | Gln |
| Arg | Leu 610 | Asp | Leu | Glu | Asn | Ala 615 | Val | Leu | Met | Gln | Glu 620 | Leu | Met | Ala | Met |
| Lys 625 | Glu | Glu | Met | Ala | Glu 630 | Leu | Lys | Ala | Gln | Leu 635 | Tyr | Leu | Leu | Glu | Lys 640 |
| Glu | Lys | Lys | Ala | Leu 645 | Glu | Leu | Lys | Leu | Ser 650 | Thr | Arg | Glu | Ala | Gln 655 | Glu |
| Gln | Ala | Tyr | Leu 660 | Val | His | Ile | Glu | His 665 | Leu | Lys | Ser | Glu | Val 670 | Glu | Glu |
| Gln | Lys | Glu 675 | | Ärg | Met | Arg | Ser 680 | Leu | Ser | Ser | Thr | Ser 685 | Ser | Gly | Ser |
| Lys | Asp 690 | Lys | Pro | Gly | Lys | Glu 695 | Cys | Ala | Asp | Ala | Ala 700 | Ser | Pro | Ala | Leu |
| Ser 705 | Leu | Ala | Glu | Leu | Arg 710 | Thr | Thr | Cys | Ser | Glu 715 | Asn | Glu | Leu | Ala | Ala 720 |
| Glu | Phe | Thr | Asn | Ala 725 | Ile | Arg | Arg | Glu | Lys 730 | Lys | Leu | Lys | Ala | Arg 735 | Val |
| Gln | Glu | Leu | Val 740 | Ser | Ala | Leu | Glu | Arg 745 | Leu | Thr | Lys | Ser | Ser 750 | Glu | Ile |
| Arg | His | Gln 755 | Gln | Ser | Ala | Glu | Phe 760 | Val | Asn | Asp | Leu | Lys 765 | Arg | Ala | Asn |
| Ser | Asn 770 | Leu | Val | Ala | Ala | Tyr 775 | Glu | Lys | Ala | Lys | Lys 780 | Lys | His | Gln | Asn |
| Lys 785 | Leu | Lys | Lys | Leu | Glu 790 | Ser | Gln | Met | | 795 | | Val | Glu | Arg | His 800 |
| | | | | | | | | | Р | age | 12 | | | | |

Glu Thr Gln Val Arg Met Leu Lys Gln Arg Ile Ala Leu Leu Glu Glu 805 810 815

Glu Asn Ser Arg Pro His Thr Asn Glu Thr Ser Leu 820 825

<210> 27

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<212> PRT

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<400> 27

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Ala Asn Arg Phe Ala Arg Lys Gly Ala Leu Arg Gln Lys Asn Val His 20 25 30

Glu Val Lys Asp His Lys Phe Ile Ala Arg Phe Phe Lys Gln Pro Thr 35 40 45

Phe Cys Ser His Cys Thr Asp Phe Ile Trp Gly Phe Gly Lys Gly Gly 50 55 60

Phe Gln Cys Gln Val Cys Cys Phe Val Val His Lys Arg Cys His Glu 65 70 75 80

Phe Val Thr Phe Ser Cys Pro Gly Ala Asp Lys Gly Pro Asp Thr Asp 85 90 95

Asp Pro Arg Ser Lys His Lys Phe Lys Ile His Thr Tyr Gly Ser Pro 100 105 110

Thr Phe Cys Asp His Cys Gly Ser Leu Leu Tyr Gly Leu Ile His Gln
115 120 125

Gly Met Lys Cys Asp Thr Cys Asp Met Asn Val His Lys Gln Cys Val 130 135 140

Ile Asn Val Pro Ser Leu Cys Gly Met Asp His Thr Glu Lys Arg Gly
145 150 155 160

Arg Ile Tyr Leu Lys Ala Glu Val Ala Asp Glu Lys Leu His Val Thr
165 170 175

Val Arg Asp Ala Lys Asn Leu Ile Pro Met Asp Pro Asn Gly Leu Ser 180 185 190

Asp Pro Tyr Val Lys Leu Lys Leu Ile Pro Asp Pro Lys Asn Glu Ser 195 200 205

Lys Gln Lys Thr Lys Thr Ile Arg Ser Thr Leu Asn Pro Gln Trp Asn 210 215 220

Glu Ser Phe Thr Phe Lys Leu Lys Pro Ser Asp Lys Asp Arg Arg Leu 225 230 235 240

| | | | | | | | | | | 6582 | 3 | | | | |
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| Ser | Val | Glu | Ile | Trp 245 | Asp | Trp | Asp | Arg | Thr 250 | Thr | Arg | Asn | Asp | Phe 255 | Met |
| Gly | Ser | Leu | Ser 260 | Phe | Gly | Val | Ser | Glu 265 | Leu | Met | Lys | Met | Pro 270 | Ala | Ser |
| Gly | Trp | Tyr 275 | Lys | Leu | Leu | Asn | Gln 280 | Glu | Glu | Gly | Glu | Tyr 285 | Tyr | Asn | Val |
| Pro | Ile 290 | Pro | Glu | Gly | Asp | Glu 295 | Glu | Gly | Asn | Met | Glu 300 | Leu | Arg | Gln | Lys |
| Phe 305 | Glu | Lys | Ala | Lys | Leu 310 | Gly | Pro | Ala | Gly | Asn 315 | Lys | Val | Ile | Ser | Pro 320 |
| Ser | Glu | Asp | Arg | Lys 325 | Gln | Pro | Ser | Asn | Asn 330 | Leu | Asp | Arg | Val | Lys 335 | Leu |
| Thr | Asp | Phe | Asn 340 | Phe | Leu | Met | Val | Leu 345 | Gly | Lys | Gly | Ser | Phe 350 | Ġly | Lys |
| Val | Met | Leu 355 | Ala | Asp | Arg | Lys | Gly 360 | Thr | Glu | Glu | Leu | Tyr 365 | Ala | Ile | Lys |
| lle | Leu 370 | Lys | Lys | Asp | Val | Val 375 | Ile | Gln | Asp | Asp | Asp 380 | Val | Glu | Cys | Thr |
| Met 385 | Val | Glu | Lys | Arg | Val 390 | Leu | Ala | Leu | Leu | Asp 395 | Lys | Pro | Pro | Phe | Leu 400 |
| Thr | Gln | Leu | His | Ser 405 | Cys | Phe | Gln | Thr | Val 410 | Asp | Arg | Leu | Tyr | Phe 415 | Val |
| Met | Glu | Tyr | Val 420 | Asn | Gly | Gly | Asp | Leu 425 | Met | Tyr | His | Ile | Gln 430 | Gln | Val |
| Gly | Lys | Phe 435 | Lys | Glu | Pro | Gln | Ala 440 | Val | Phe | Tyr | Ala | Ala 445 | Glu | Ile | Ser |
| Ile | Gly 450 | Leu | Phe | Phe | Leu | His 455 | Lys | Arg | Gly | Ile | Ile 460 | Tyr | Arg | Asp | Leu |
| Lys 465 | Leu | Asp | Asn | Val | Met 470 | Leu | Asp | Ser | Glu | Gly 475 | His | Ile | Lys | Ile | Ala 480 |
| Asp | Phe | Gly | Met | Cys 485 | Lys | Glu | His | Met | Met 490 | Asp. | Gly | Val | Thr | Thr 495 | Arg |
| Thr | Phe | Cys | Gly 500 | Thr | Pro | Asp | Tyr | Ile 505 | Ala | Pro | Glu | Ile | Ile 510 | Ala | Tyr |
| Gln | Pro | Tyr 515 | Gly | Lys | Ser | Val | Asp 520 | Trp | Trp | Ala | Tyr | Gly 525 | Val | Leu | Leu |
| Tyr | Glu 530 | Met | Leu | Ala | Gly | Gln 535 | Pro | Pro | Phe | Asp | Gly 540 | Glu | Asp | Glu | Asp |
| Glu 545 | Leu | Phe | Gln | Ser | Ile 550 | Met | Glu | His | | 555 | | Tyr | Pro | Lys | Ser 560 |
| | | | | | | | | | P | age | 14 | | | | |

 Leu
 Ser
 Lys
 Glu
 Ala 565
 Val
 Ser
 Ile
 Cys
 Lys 570
 Gly
 Leu
 Met
 Thr
 Lys 575
 His 575

 Pro
 Ala Lys
 Arg 580
 Leu
 Gly
 Cys
 Glu
 Gly
 Glu
 Gly
 Glu
 Arg 590
 Val
 Arg 600
 Arg 600
 Arg 790
 Arg 790

<210> 28 <211> 471 <212> PRT <213> human

<400> 28

Met Asp Ile Leu Cys Glu Glu Asn Thr Ser Leu Ser Ser Thr Thr Asn 1 5 10 15

Ser Leu Met Gln Leu Asn Asp Asp Thr Arg Leu Tyr Ser Asn Asp Phe 20 25 30

Asn Ser Gly Glu Ala Asn Thr Ser Asp Ala Phe Asn Trp Thr Val Asp $35 \hspace{1cm} 40 \hspace{1cm} 45$

Ser Glu Asn Arg Thr Asn Leu Ser Cys Glu Gly Cys Leu Ser Pro Ser 50 60

Cys Leu Ser Leu Leu His Leu Gln Glu Lys Asn Trp Ser Ala Leu Leu 65 70 75 80

Thr Ala Val Val Ile Ile Leu Thr Ile Ala Gly Asn Ile Leu Val Ile 85 90 95

Met Ala Val Ser Leu Glu Lys Lys Leu Gln Asn Ala Thr Asn Tyr Phe 100 105 110

Leu Met Ser Leu Ala Ile Ala Asp Met Leu Leu Gly Phe Leu Val Met 115 120 125

Pro Val Ser Met Leu Thr Ile Leu Tyr Gly Tyr Arg Trp Pro Leu Pro 130 135 140

| Ser 145 | Lys | Leu | Cys | Ala | Val 150 | Trp | Ile | Tyr | | 6582 Asp 155 | _ | Leu | Phe | Ser | Thr 160 |
|------------|-----|-----|-----|------------|------------|-----|-----|-----|------------|--------------------|-----|-----|-----|------------|------------|
| Ala | Ser | Ile | Met | His 165 | Leu | Cys | Ala | Ile | Ser 170 | Leu | Asp | Arg | Tyr | Val 175 | Ala |

Ile Gln Asn Pro Ile His His Ser Arg Phe Asn Ser Arg Thr Lys Ala 180 185 190

Phe Leu Lys Ile Ile Ala Val Trp Thr Ile Ser Val Gly Ile Ser Met 195 200 205

Pro Ile Pro Val Phe Gly Leu Gln Asp Asp Ser Lys Val Phe Lys Glu 210 215 220

Gly Ser Cys Leu Leu Ala Asp Asp Asn Phe Val Leu Ile Gly Ser Phe 225 230 235 240

Val Ser Phe Phe Ile Pro Leu Thr Ile Met Val Ile Thr Tyr Phe Leu 245 250 255

Thr Ile Lys Ser Leu Gln Lys Glu Ala Thr Leu Cys Val Ser Asp Leu 260 265 270

Gly Thr Arg Ala Lys Leu Ala Ser Phe Ser Phe Leu Pro Gln Ser Ser 275 280 285

Leu Ser Ser Glu Lys Leu Phe Gln Arg Ser Ile His Arg Glu Pro Gly 290 295 300

Ser Tyr Thr Gly Arg Arg Thr Met Gln Ser Ile Ser Asn Glu Gln Lys 305 310 315

Ala Cys Lys Val Leu Gly Ile Val Phe Phe Leu Phe Val Val Met Trp 325 330 . 335

Cys Pro Phe Phe Ile Thr Asn Ile Met Ala Val Ile Cys Lys Glu Ser 340 345 350

. Cys Asn Glu Asp Val Ile Gly Ala Leu Leu Asn Val Phe Val Trp Ile 355 360 365

Gly Tyr Leu Ser Ser Ala Val Asn Pro Leu Val Tyr Thr Leu Phe Asn 370 375 380

Lys Thr Tyr Arg Ser Ala Phe Ser Arg Tyr Ile Gln Cys Gln Tyr Lys 385 390 395 400

Glu Asn Lys Lys Pro Leu Gln Leu Ile Leu Val Asn Thr Ile Pro Ala 405 410 415

Leu Ala Tyr Lys Ser Ser Gln Leu Gln Met Gly Gln Lys Lys Asn Ser 420 425 430

Lys Gln Asp Ala Lys Thr Thr Asp Asn Asp Cys Ser Met Val Ala Leu 435 440 445

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Glu Gln Gly Asn Lys Leu His Trp Ala Ala Leu Leu Ile Leu Met Val
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Pro Ala Trp Leu Phe Leu Asp Val Leu Phe Ser Thr Ala Ser Ile Met 130 135 140

His Leu Cys Ala Ile Ser Val Asp Arg Tyr Ile Ala Ile Lys Lys Pro 145 150 155 160

Ile Gln Ala Asn Gln Tyr Asn Ser Arg Ala Thr Ala Phe Ile Lys Ile 165 170 175

Thr Val Val Trp Leu Ile Ser Ile Gly Ile Ala Ile Pro Val Pro Ile 180 185 190

Lys Gly Ile Glu Thr Asp Val Asp Asn Pro Asn Asn Ile Thr Cys Val 195 200 205

Leu Thr Lys Glu Arg Phe Gly Asp Phe Met Leu Phe Gly Ser Leu Ala 210 215 220

Ala Phe Phe Thr Pro Leu Ala Ile Met Ile Val Thr Tyr Phe Leu Thr 225 230 235 240

Ile His Ala Leu Gln Lys Lys Ala Tyr Leu Val Lys Asn Lys Pro Pro 245 250 255

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J5

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Gln Ile Asp Leu L
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Asn Phe Pro Gly V

Gly Ser Arg Glu G
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Val Pro Met Gly S
115

Glu Ser Thr Gly T
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Leu Ala Asp Leu A
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Gln Ile Asp Leu Leu Glu Arg Leu Lys Glu Leu Asn Leu Asp Ser Ser 65 70 75 80

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Glu Ala Glu Arg Ser Ser Gln Asn Lys His Glu Thr Gly Ser His Asp 245 250 255

Ala Glu Arg Gln Asn Glu Gly Gln Gly Val Gly Glu Ile Asn Met Ala 260 265 270

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Ala Ser Val Leu Ser Ser Ser Ser Thr His Ser Ala Pro Arg Arg Leu 290 295 300

Thr Ser His Leu Gly Thr Lys Val Glu Met Val Tyr Ser Leu Leu Ser 305 310 315 320

Met Leu Gly Thr His Asp Lys Asp Asp Met Ser Arg Thr Leu Leu Ala 325 330 335

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| Ser | Leu | Thr 675 | Ile | Val | Ser | Asn | Ala 680 | Cys | Gly | Thr | Leu | Trp 685 | Asn | Leu | Ser |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
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| Ser 705 | Met | Leu | Lys | Asn | Leu 710 | Ile | His | Ser | Lys | His 715 | Lys | Met | Ile | Ala | Met 720 |
| Gly | Ser | Ala | Ala | Ala 725 | Leu | Arg | Asn | Leu | Met 730 | Ala | Asn | Arg | Pro | Ala 735 | Lys |
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| His | Val | Arg 755 | Lys | Gln | Lys | Ala | Leu 760 | Glu | Ala | Glu | Leu | Asp 765 | Ala | Gln | His |
| Leu | Ser 770 | Glu | Thr | Phe | Asp | Asn 775 | Ile | Asp | Asn | Ile | Ser 780 | Pro | Lys | Ala | Ser |
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| Gly | Asn | Met | Thr 820 | Val | Leu | Ser | Pro | Tyr 825 | Leu | Asn | Thr | Thr | Val 830 | Leu | Pro |
| Ser | Ser | Ser 835 | Ser | Ser | Arg | Gly | Ser 840 | Leu | Asp | Ser | Ser | Arg 845 | Ser | Glu | Lys |
| Asp | Arg 850 | Ser | Leu | Glu | Arg | Glu 855 | Arg | Gly | Ile | Gly | Leu 860 | Gly | Asn : | Tyr | His |
| Pro 865 | Ala | Thr | Glu | Asn | Pro 870 | Gly | Thr | Ser | Ser | Lys 875 | Arg | Gly | Leu | Gln | Ile 880 |
| Ser | Thr | Thr | Ala | Ala 885 | Gln | Ile | Ala | Lys | Val 890 | Met | Glu | Glu | Val | Ser 895 | Ala |
| Ile | His | Thr | Ser 900 | Gln | Glu | Asp | Arg | Ser 905 | Ser | Gly | Ser | Thr | Thr 910 | Glu | Leu |
| His | Cys | Val 915 | Thr | Asp | Glu | Arg | Asn 920 | Ala | Leu | Arg | Arg | Ser 925 | Ser | Ala | Ala |
| His | Thr 930 | His | Ser | Asn | Thr | Tyr 935 | Asn | Phe | Thr | Lys | Ser 940 | Glu | Asn | Ser | Asn |
| Arg 945 | Thr | Cys | Ser | Met | Pro 950 | Tyr | Ala | Lys | Leu | Glu 955 | Tyr | Lys | Arg | Ser | Ser 960 |
| Asn | Asp | Ser | Leu | Asn 965 | Ser | Val | Ser | Ser | Ser 970 | Asp | Gly | Tyr | Gly | Lys 975 | Arg |
| Gly | Gln | Met | Lys | Pro | Ser | Ile | Glu | Ser | | Ser age | | Asp | Asp | Glu | Ser |

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- Gln Ser Pro Ser Gln Asn Glu Arg Trp Ala Arg Pro Lys His Ile Ile 1050
- Glu Asp Glu Ile Lys Gln Ser Glu Gln Arg Gln Ser Arg Asn Gln Ser 1065
- Thr Thr Tyr Pro Val Tyr Thr Glu Ser Thr Asp Asp Lys His Leu Lys
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- His Glu Glu Glu Glu Arg Pro Thr Asn Tyr Ser Ile Lys Tyr Asn Glu 1160
- Glu Lys Arg His Val Asp Gln Pro Ile Asp Tyr Ser Ile Leu Lys Ala 1175
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- Ser Ser Gly Gln Ser Ser Lys Thr Glu His Met Ser Ser Ser Glu 1205 1210
- Asn Thr Ser Thr Pro Ser Ser Asn Ala Lys Arg Gln Asn Gln Leu His
- Pro Ser Ser Ala Gln Ser Arg Ser Gly Gln Pro Gln Lys Ala Ala Thr
- Cys Lys Val Ser Ser Ile Asn Gln Glu Thr Ile Gln Thr Tyr Cys Val 1250 1255
- Glu Asp Thr Pro Ile Cys Phe Ser Arg Cys Ser Ser Leu Ser Ser Leu 1275
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- Ala Glu Lys Thr Ile Asp Ser Glu Lys Asp Leu Leu Asp Asp Ser Asp 1555 1560 1565
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- Thr Asp Glu Ala Gln Gly Gly Lys Thr Ser Ser Val Thr Ile Pro Glu
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- Lys Asp Ser Lys Lys Gln Asn Leu Lys Asn Asn Ser Lys Asp Phe Asn 1810 1815 1820
- Asp Lys Leu Pro Asn Asn Glu Asp Arg Val Arg Gly Ser Phe Ala Phe 1825 1830 1835 1840
- Asp Ser Pro His His Tyr Thr Pro Ile Glu Gly Thr Pro Tyr Cys Phe
 1845 1850 1855
- Ser Arg Asn Asp Ser Leu Ser Ser Leu Asp Phe Asp Asp Asp Val 1860 1865 1870
- Asp Leu Ser Arg Glu Lys Ala Glu Leu Arg Lys Ala Lys Glu Asn Lys 1875 1880 1885
- Glu Ser Glu Ala Lys Val Thr Ser His Thr Glu Leu Thr Ser Asn Gln 1890 1895 1900
- Gln Ser Ala Asn Lys Thr Gln Ala Ile Ala Lys Gln Pro Ile Asn Arg 1905 1910 1915 1920
- Gly Gln Pro Lys Pro Ile Leu Gln Lys Gln Ser Thr Phe Pro Gln Ser Page 24

. Ser Lys Asp Ile Pro Asp Arg Gly Ala Ala Thr Asp Glu Lys Leu Gln

Asn Phe Ala Ile Glu Asn Thr Pro Val Cys Phe Ser His Asn Ser Ser 1955 1960 1965

1945

Leu Ser Ser Leu Ser Asp Ile Asp Gln Glu Asn Asn Asn Lys Glu Asn 1970 1975 1980

Glu Pro Ile Lys Glu Thr Glu Pro Pro Asp Ser Gln Gly Glu Pro Ser 1985 1990 1995 2000

Lys Pro Gln Ala Ser Gly Tyr Ala Pro Lys Ser Phe His Val Glu Asp 2005 2010 2015

Thr Pro Val Cys Phe Ser Arg Asn Ser Ser Leu Ser Ser Leu Ser Ile 2020 2025 2030

Asp Ser Glu Asp Asp Leu Leu Gln Glu Cys Ile Ser Ser Ala Met Pro 2035 2040 2045

Lys Lys Lys Pro Ser Arg Leu Lys Gly Asp Asn Glu Lys His Ser 2050 2055 2060

Pro Arg Asn Met Gly Gly Ile Leu Gly Glu Asp Leu Thr Leu Asp Leu 2065 2070 2075 2080

Lys Asp Ile Gln Arg Pro Asp Ser Glu His Gly Leu Ser Pro Asp Ser 2085 2090 2095

Glu Asn Phe Asp Trp Lys Ala Ile Gln Glu Gly Ala Asn Ser Ile Val 2100 2105 2110

Ser Ser Leu His Gln Ala Ala Ala Ala Cys Leu Ser Arg Gln Ala 2115 2120 2125

Ser Ser Asp Ser Asp Ser Ile Leu Ser Leu Lys Ser Gly Ile Ser Leu 2130 2135 2140

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Ser Asn Lys Gly Pro Arg Ile Leu Lys Pro Gly Glu Lys Ser Thr Leu 2165 2170 2175

Glu Thr Lys Lys Ile Glu Ser Glu Ser Lys Gly Ile Lys Gly Gly Lys 2180 2185 2190

Lys Val Tyr Lys Ser Leu Ile Thr Gly Lys Val Arg Ser Asn Ser Glu 2195 2200 2205

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- Gly Ala Lys Pro Ser Val Lys Ser Glu Leu Ser Pro Val Ala Arg Gln 2275 2280 2285
- Thr Ser Gln Ile Gly Gly Ser Ser Lys Ala Pro Ser Arg Ser Gly Ser 2290 2295 2300
- Arg Asp Ser Thr Pro Ser Arg Pro Ala Gln Gln Pro Leu Ser Arg Pro 2305 2310 2315 2320
- Ile Gln Ser Pro Gly Arg Asn Ser Ile Ser Pro Gly Arg Asn Gly Ile 2325 2330 2335
- Ser Pro Pro Asn Lys Ile Ser Gln Leu Pro Arg Thr Ser Ser Pro Ser 2340 2345 2350
- Thr Ala Ser Thr Lys Ser Ser Gly Ser Gly Lys Met Ser Tyr Thr Ser 2355 2360 2365
- Pro Gly Arg Gln Met Ser Gln Gln Asn Leu Thr Lys Gln Thr Gly Leu 2370 2380
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- Thr Pro Val Leu Ser Pro Ser Leu Pro Asp Met Ser Leu Ser Thr His
 2485 2490 2495
- Ser Ser Val Gln Ala Gly Gly Trp Arg Lys Leu Pro Pro Asn Leu Ser 2500 2505 2510
- Pro Thr Ile Glu Tyr Asn Asp Gly Arg Pro Ala Lys Arg His Asp Ile 2515 2520 2525
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- Val Ser Thr Trp Arg Arg Thr Gly Ser Ser Ser Ser Ile Leu Ser Ala 2565 2570 2575
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- Lys Ala Asn Pro Asn Ile Lys Asp Ser Lys Asp Asn Gln Ala Lys Gln 2690 2695 2700
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- Glu Ile Lys Pro Gly Gln Asn Asn Pro Val Pro Val Ser Glu Thr Asn 2740 2745 2750
- Glu Ser Ser Ile Val Glu Arg Thr Pro Phe Ser Ser Ser Ser Ser Ser Ser 2755
- Lys His Ser Ser Pro Ser Gly Thr Val Ala Ala Arg Val Thr Pro Phe 2770 2780
- Asn Tyr Asn Pro Ser Pro Arg Lys Ser Ser Ala Asp Ser Thr Ser Ala 2785 2790 2795 2800
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